

β1a1

NcoI
 -2 CCATGGGCAGAGACTCCCCAAGGGATTTCGTGTACCAGTTCAAGGGCCTGTGCTACTACACC 60
 M G R D S P R D F V Y Q F K G L C Y Y T
 61 AACGGGACGCAGCGCATAACGGGATGTGATCAGATACATCTACAACCAGGAGGAGTACCTG 120
 N G T Q R I R D V I R Y I Y N Q E E Y L
 121 CGCTACGACAGCGACGTGGGCGAGTACCGCGCGCTGACCGAGCTGGGGCGGCCCTCAGCC 180
 R Y D S D V G E Y R A L T E L G R P S A
 181 GAGTACTTTAACAAGCAGTACCTGGAGCAGACGCGGGCCGAGCTGGACACGGTCTGCAGA 240
 E Y F N K Q Y L E Q T R A E L D T V C R
 241 CACAACTACGAGGGGTCGGAGGTCCGCACCTCCCTGCGGCGGCTTGGAGGTCAAGACGAC 300
 H N Y E G S E V R T S L R R L G G Q D D
 301 ATTGAGGCCGACCACGTAGCCGCCTATGGTATAAATATGTATCAGTATTATGAATCCAGA 360
 I E A D H V A A Y G I N M Y Q Y Y E S R
 361 GGCCAGTTTACACATGAATTTGATGGTGACGAGGAATTCTATGTGGACTTGGATAAGAAG 420
 G Q F T H E F D G D E E F Y V D L D K K
 421 GAGACCATCTGGAGGATCCCCGAGTTTGGACAGCTGACAAGCTTTGACCCCCAAGGTGGA 480
 E T I W R I P E F G Q L T S F D P Q G G
 481 CTTCAAAATATAGCTATAATAAAACACAATTTGGAAATCTTGATGAAGAGGTCAAATTCA 540
 L Q N I A I I K H N L E I L M K R S N S
 541 ACCCAAGCTGTCAACTAACTCGAG
 T Q A V N end

FIG. 1A

FIG. 1B

$\beta 1\alpha 1$ /MBP-72-89

Neol

CCATGGGCAGAGACTCCCCACAGAGAGCCAGAGGACTCAGGATGAGAACCCAGTGGTGCACCTCGGAGGTGGAGGCTCACTAGTGGCCCCGAGGCTCT

M G R D S P Q K S Q R T Q D E N P V V H F G G G S L V P R G S

GGAGGTGGAGGCTCC

G G G G S

SpeI

---linker---|-----thrombin----

FIG. 1C

$\beta 1\alpha 1$ /MBP-55-69

Neol

CCATGGGCAGAGACTCCCGGCGAGGATTCGCATCATGCGCGCGGACGACCCACTACGGTGGAGGTGGAGGCTCACTAGTG

M G R D S S G K D S H A A R T T H Y G G G G S L V

SpeI

FIG. 1D

$\beta 1\alpha 1$ /CM-2

Neol

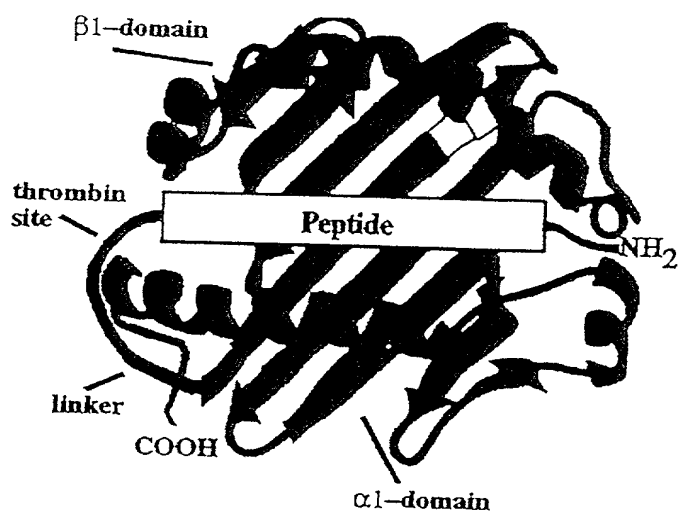
CCATGGGCAGAGACTCCAACTGGACTGCAGTCCGCTCTGGAAGAGCTGAGCTTCCTGGACACGAGGTGGAGGCTCACTAGTG

M G R D S K L E L Q S A L E E A E A S L E H G G G S L V

SpeI



a. RT1.B



b. $\beta 1\alpha 1$ /peptide

FIG. 2
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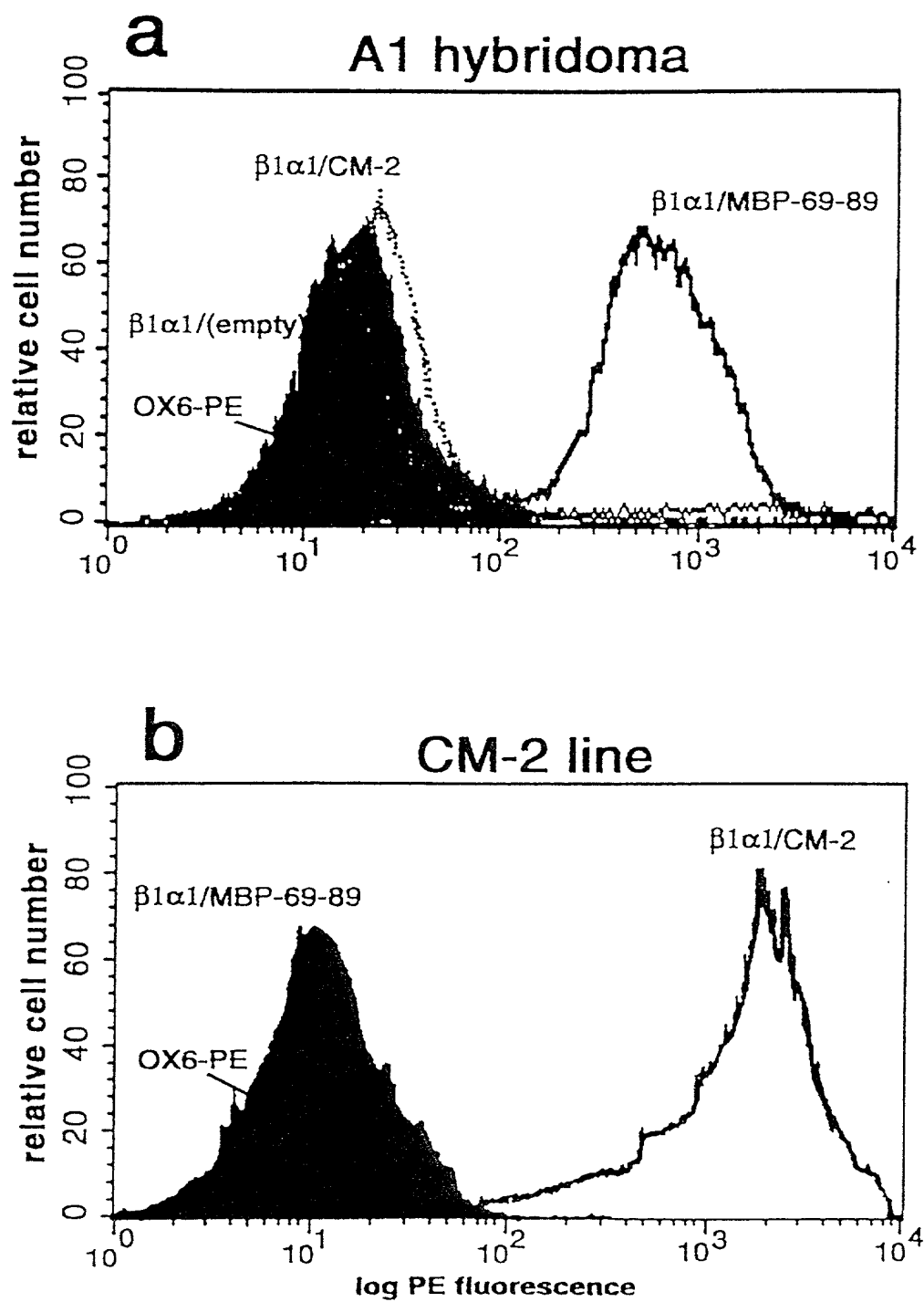


FIG. 3

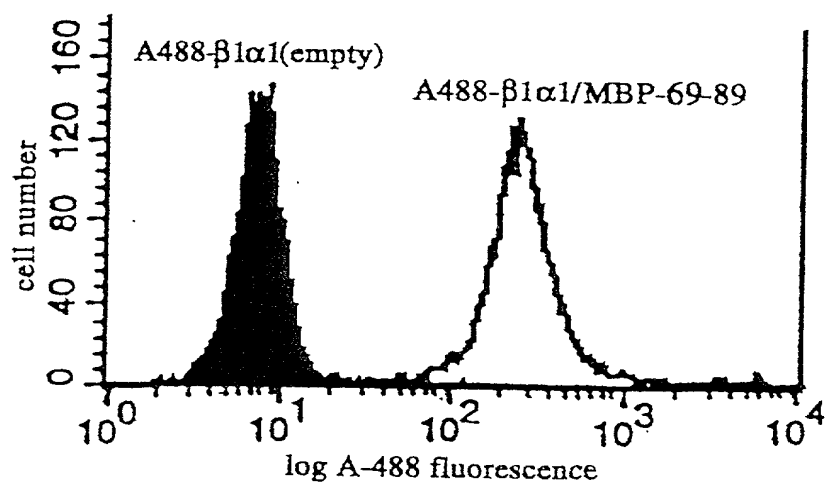


FIG. 4
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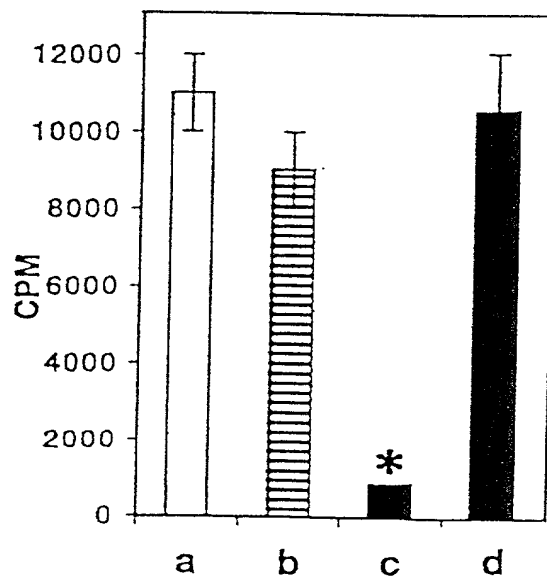


FIG. 5
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20250624050

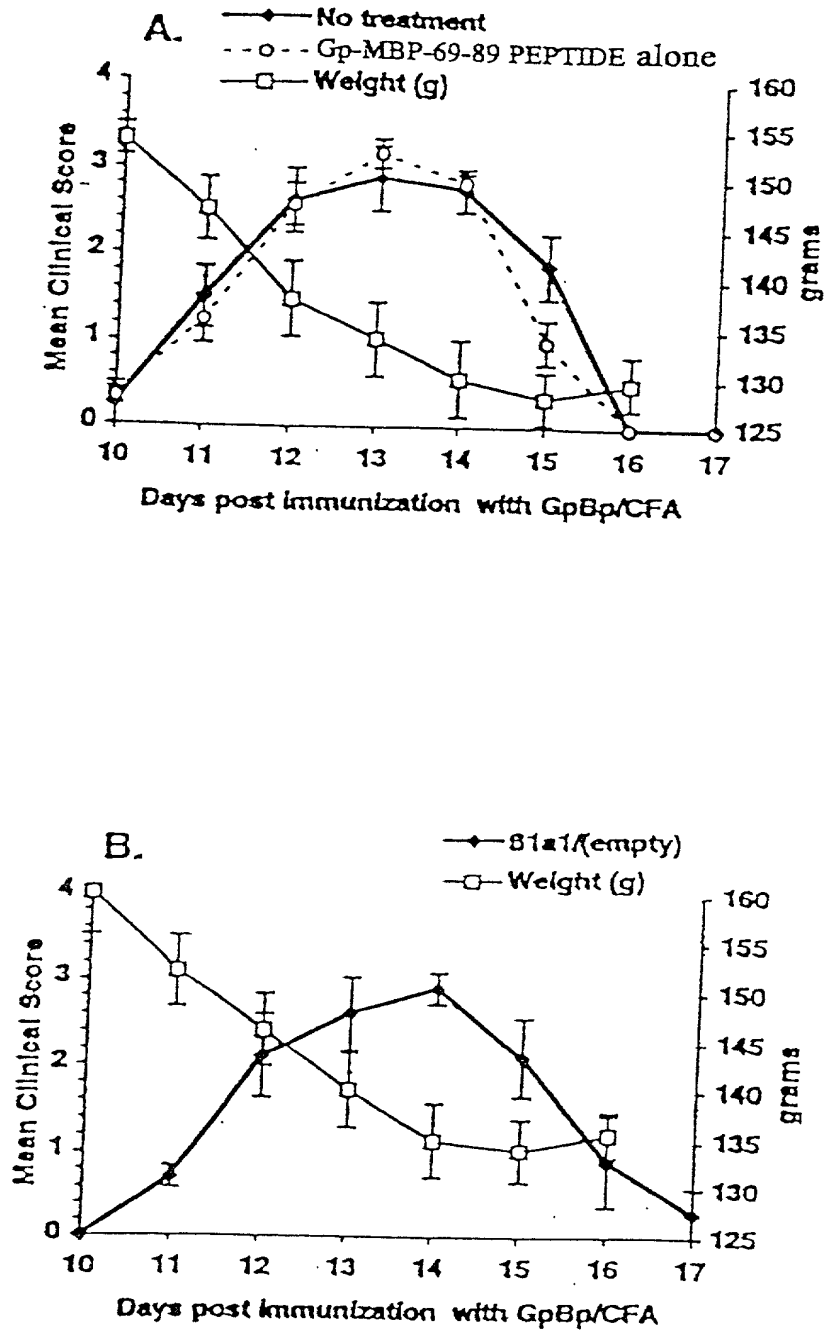


FIG. 6A
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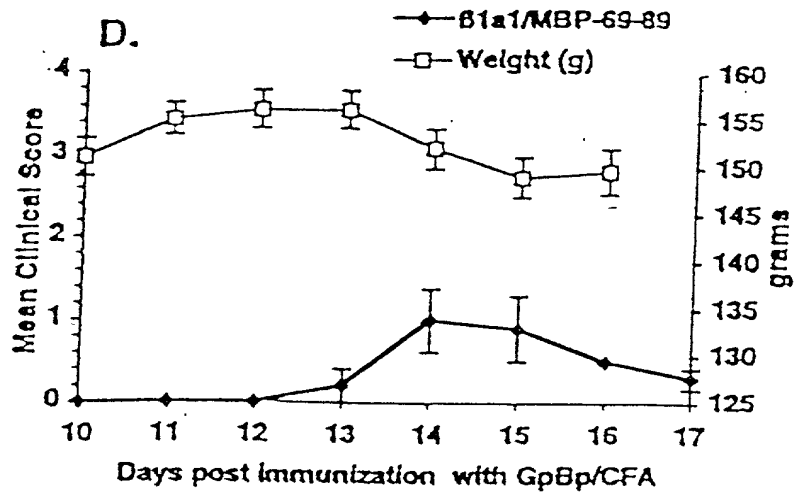
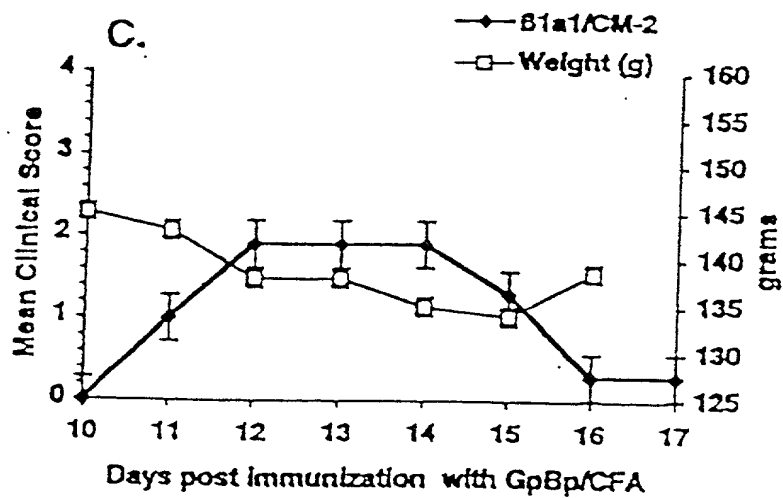


FIG. 6B
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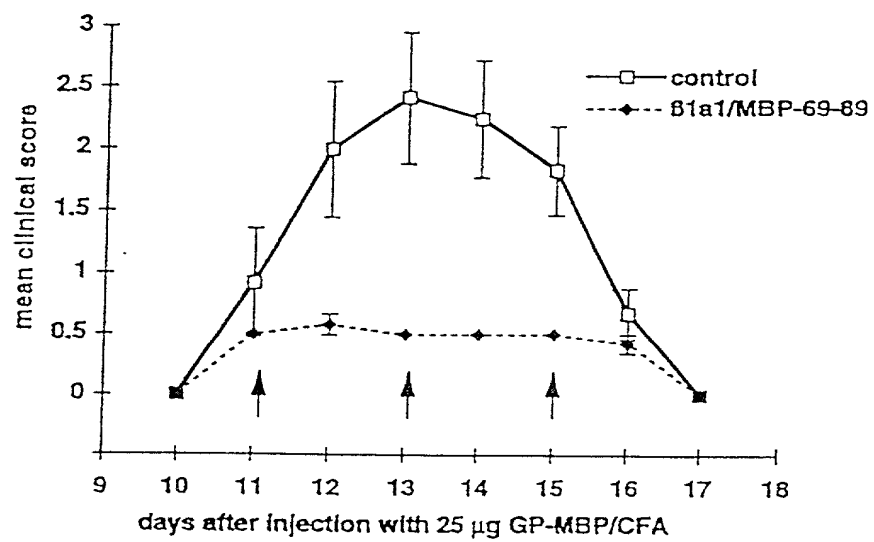


FIG. 7
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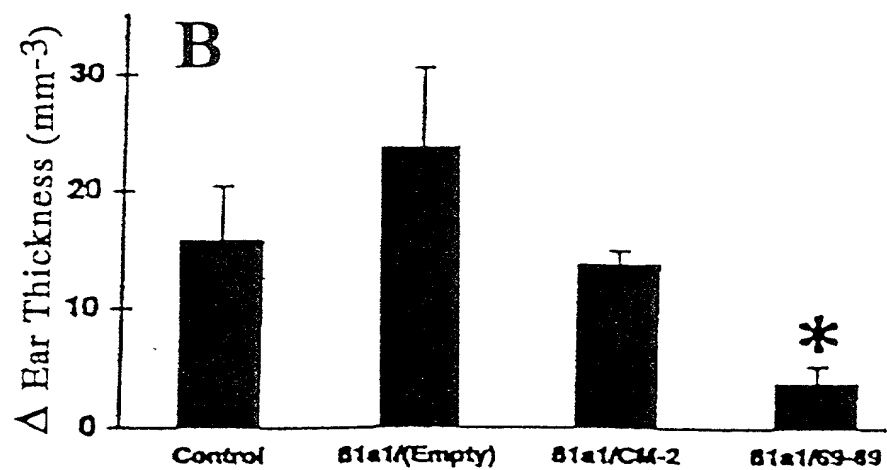
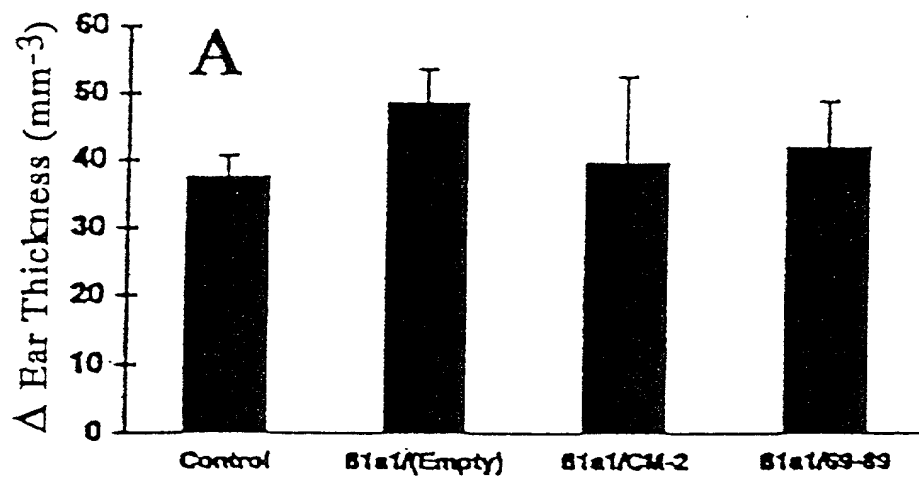


FIG. 8
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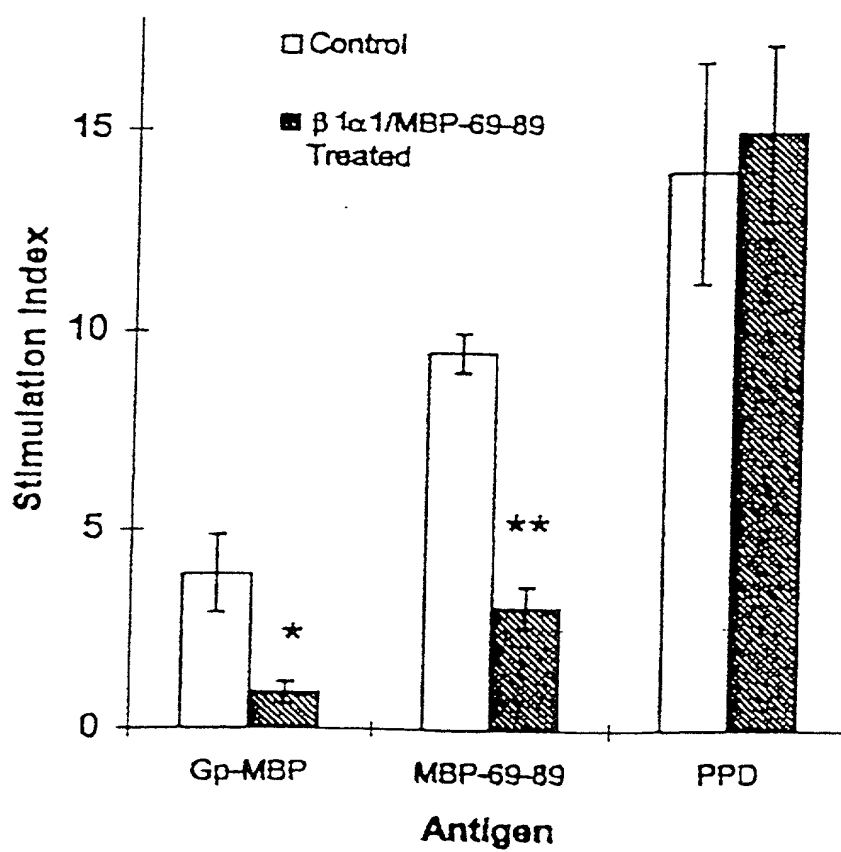


FIG. 9
11/15

β 1 domain:
 ARG4-PRO5-ARG6-PHE7-LEU8-TRP9-GLN10-LEU11-LYS12-PHE13-GLU14-CYS15-
 HIS16-PHE17-PHE18-ASN19-GLY20-THR21-GLU22-ARG23-VAL24-ARG25-LEU26-
 LEU27-GLU28-ARG29-CYS30-ILE31-TYR32-ASN33-GLN34-GLU35-GLU36-SER37-
 VAL38-ARG39-PHE40-ASP41-SER42-ASP43-VAL44-GLY45-GLU46-TYR47-ARG48-
 ALA49-VAL50-THR51-GLU52-LEU53-GLY54-ARG55-PRO56-ASP57-ALA58-GLU59-
 TYR60-TRP61-ASN62-SER63-GLN64-LYS65-ASP66-LEU67-LEU68-GLU69-GLN70-
 ARG71-ARG72-ALA73-ALA74-VAL75-ASP76-THR77-TYR78-CYS79-ARG80-HIS81-
 ASN82-TYR83-GLY84-VAL85-GLY86-GLU87-SER88-PHE89-THR90-VAL91-GLN92-
 ARG93-ARG94-VAL95
 α 1 domain:
 GLU3-GLU4-HIS5-VAL6-ILE7-ILE8-GLN9-ALA10-GLU11-PHE12-TYR13-LEU14-
 ASN15-PRO16-ASP17-GLN18-SER19-GLY20-GLU21-PHE22-MET23-PHE24-ASP25-
 PHE26-ASP27-GLY28-ASP29-GLU30-ILE31-PHE32-HIS33-VAL34-ASP35-MET36-
 ALA37-LYS38-LYS39-GLU40-THR41-VAL42-TRP43-ARG44-LEU45-GLU46-GLU47-
 PHE48-GLY49-ARG50-PHE51-ALA52-SER53-PHE54-GLU55-ALA56-GLN57-GLY58-
 ALA59-LEU60-ALA61-ASN62-ILE63-ALA64-VAL65-ASP66-LYS67-ALA68-ASN69-
 LEU70-GLU71-ILE72-MET73-THR74-LYS75-ARG76-SER77-ASN78-TYR79-THR80-
 PRO81-ILE82-THR83-ASN84

FIG. 10A
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β 1 domain:
ARG4-PRO5-TRP6-PHE7-LEU8-GLU9-TYR10-CYS11-LYS12-SER13-GLU14-CYS15-
HIS16-PHE17-TYR18-ASN19-GLY20-THR21-GLN22-ARG23-VAL24-ARG25-LEU26-
LEU27-VAL28-ARG29-TYR30-PHE31-TYR32-ASN33-LEU34-GLU35-GLU36-ASN37-
ALA49-VAL50-THR51-GLU52-LEU53-GLY54-ARG55-PRO56-ASP57-ALA58-GLU59-
ASN60-TRP61-ASN62-SER63-GLN64-PRO65-GLU66-PHE67-LEU68-GLU69-GLN70-
LYS71-ARG72-ALA73-GLU74-VAL75-ASP76-THR77-VAL78-CYS79-ARG80-HIS81-
ASN82-TYR83-GLU84-ILE85-PHE86-ASP87-ASN88-PHE89-LEU90-VAL91-PRO92-
ARG93-ARG94-VAL95

α 1 domain:
GLU3-GLU4-HIS5-THR6-ILE7-ILE8-GLN9-ALA10-GLU11-PHE12-TYR13-LEU14-
LEU15-PRO16-ASP17-LYS18-ARG19-GLY20-GLU21-PHE22-MET23-PHE24-ASP25-
PHE26-ASP27-GLY28-ASP29-GLU30-ILE31-PHE32-HIS33-VAL34-ASP35-ILE36-
GLU37-LYS38-SER39-GLU40-THR41-ILE42-TRP43-ARG44-LEU45-GLU46-GLU47-
PHE48-ALA49-LYS50-PHE51-ALA52-SER53-PHE54-GLU55-ALA56-GLN57-GLY58-
ALA59-LEU60-ALA61-ASN62-ILE63-ALA64-VAL65-ASP66-LYS67-ALA68-ASN69-
LEU70-ASP71-VAL72-MET73-LYS74-GLU75-ARG76-SER77-ASN78-ASN79-THR80-
PRO81-ASP82-ALA83-ASN84

FIG. 10B
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β 1 domain:
 MET(-2)-GLY(-1)-ARG1-ASP2-SER3-PRO4-ARG5-ASP6-PHE7-VAL8-TYR9-
 GLN10-PHE11-LYS12-GLY13-LEU14-CYS15-TYR16-TYR17-THR18-ASN19-GLY20-
 THR21-GLN22-ARG23-ILE24-ARG25-ASP26-VAL27-ILE28-ARG29-TYR30-ILE31-
 TYR32-ASN33-GLN34-GLU35-GLU36-TYR37-LEU38-ARG39-TYR40-ASP41-SER42-
 ASP43-VAL44-GLY45-GLU46-TYR47-ARG48-ALA49-LEU50-THR51-GLU52-LEU53-
 GLY54-ARG55-PRO56-SER57-ALA58-GLU59-TYR60-TRP61-ASN62-SER63-GLN64-
 LYS65-GLN66-TYR67-LEU68-GLU69-GLN70-THR71-ARG72-ALA73-GLU74-LEU75-
 ASP76-THR77-VAL78-CYS79-ARG80-HIS81-ASN82-TYR83-GLU84-GLY85-SER86-
 GLU87-VAL88-ARG89-THR90-SER91-LEU92-ARG93-ARG94-LEU95

α 1 domain:
 ALA2-ASP3-HIS4-VAL5-ALA6-ALA7-TYR8-GLY9-ILE10-ASN11-MET12-TYR13-
 GLN14-TYR15-TYR16-GLU17-SER18-ARG19-GLY20-GLN21-PHE22-THR23-HIS24-
 GLU25-PHE26-ASP27-GLY28-ASP29-GLU30-GLU31-PHE32-TYR33-VAL34-ASP35-
 LEU36-ASP37-LYS38-LYS39-GLU40-THR41-ILE42-TRP43-ARG44-ILE45-PRO46-
 GLU47-PHE48-GLY49-GLN50-LEU51-THR52-SER53-PHE54-ASP55-PRO56-GLN57-
 GLY58-GLY59-LEU60-GLN61-ASN62-ILE63-ALA64-ILE65-ILE66-LYS67-HIS68-
 ASN69-LEU70-GLU71-ILE72-LEU73-MET74-LYS75-ARG76-SER77-ASN78-SER79-
 THR80-GLN81-ALA82-VAL83-ASN84

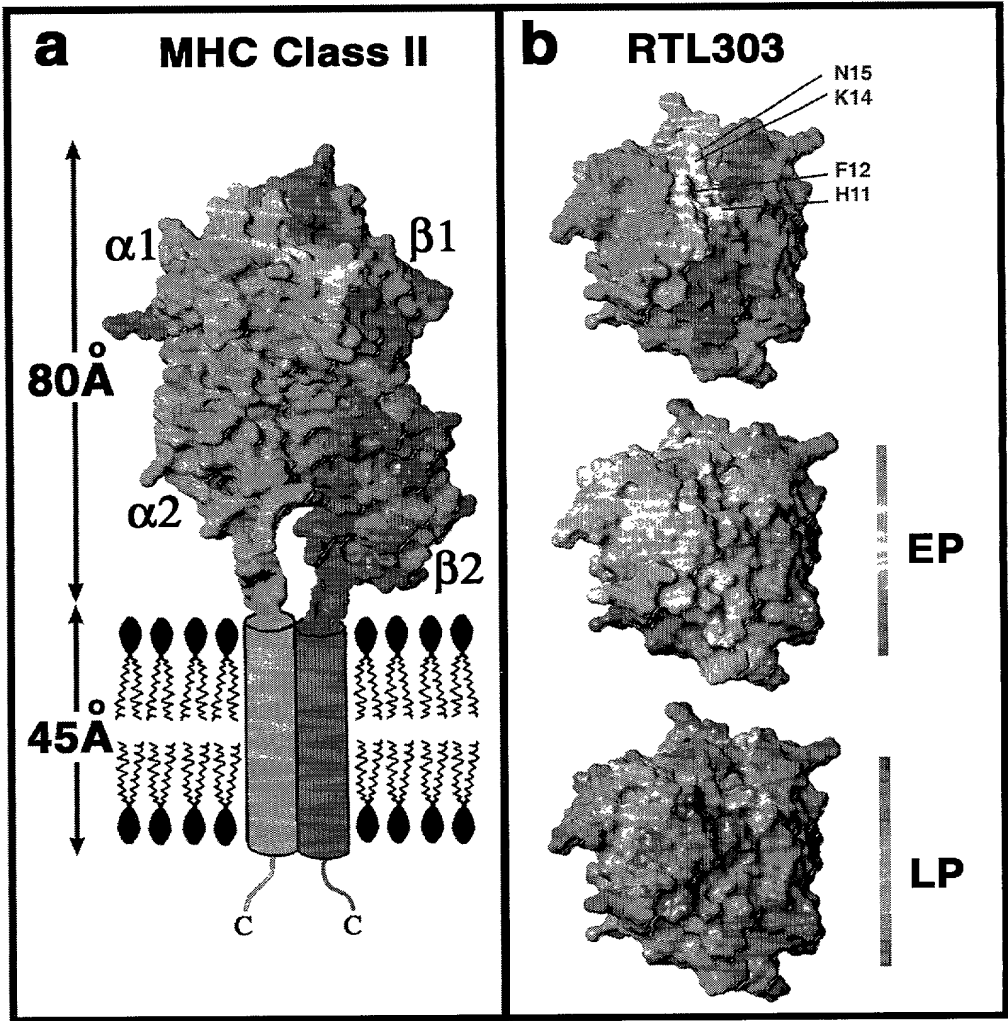
$\alpha 1$ domain:
GLY1-SER2-HIS3-SER4-MET5-ARG6-TYR7-PHE8-TYR9-THR10-ALA11-MET12-
SER13-ARG14-PRO15-GLY16-ARG17-GLY18-GLU19-PRO20-ARG21-PHE22-ILE23-
ALA24-VAL25-GLY26-TYR27-VAL28-ASP29-ASP30-THR31-GLN32-PHE33-VAL34-
ARG35-PHE36-ASP37-SER38-ASP39-ALA40-ALA41-SER42-PRO43-ARG44-THR45-
GLU46-PRO47-ARG48-PRO49-PRO50-TRP51-ILE52-GLU53-GLN54-GLU55-GLY56-
PRO57-GLU58-TYR59-TRP60-ASP61-ARG62-ASN63-THR64-GLN65-ILE66-PHE67-
LYS68-THR69-ASN70-THR71-GLN72-THR73-TYR74-ARG75-GLU76-ASN77-LEU78-
ARG79-ILE80-ALA81-LEU82-ARG83-TYR84-

$\alpha 2$ domain:
TYR85-ASN86-GLN87-SER88-GLU89-ALA90-GLY91-SER92-HIS93-ILE94-ILE95-
GLN96-ARG97-MET98-TYR99-GLY100-CYS101-ASP102-LEU103-GLY104-PRO105-
ASP106-GLY107-ARG108-LEU109-LEU110-ARG111-GLY112-HIS113-ASP114-
GLN115-SER116-ALA117-TYR118-ASP119-GLY120-LYS121-ASP122-TYR123
ILE124-ALA125-LEU126-ASN127-GLU128-ASP129-LEU130-SER131-SER132-
TRP133-THR134-ALA135-ALA136-ASP137-THR138-ALA139-ALA140-GLN141-
ILE142-THR143-GLN144-ARG145-LYS146-TRP147-GLU148-ALA149-ALA150-
ARG151-VAL152-ALA153-GLU154-GLN155-LEU156-ARG157-ALA158-TYR159-
LEU160-GLU161-GLY162-LEU163-CYS164-VAL165-GLU166-TRP167-LEU168-
ARG169-ARG170-TYR171-LEU172-GLU173-ASN174-GLY175-LYS176-GLU177-
THR178-LEU179-GLN180-ARG181-ALA182-ASP183-PRO184

FIG. 11
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FIG. 12

FIG. 12



NcoI
CCATGGGGACACCCGAGAAACCCGGTGTTCACCTCTTCAAAAACATCGTTACCCCGCTGGAGGTGGAGGCT**ACTAGT**GCCCGGAGGC
-2
M G D T R E N P V V H F F K N I V T P R G G G S L V P R G
10
TCTGGAGGTGGAGGCCACGTTCTCTGTGGAGCCTAAGAGGGAGTGTCAATTTCTCAATGGACGGAGCGGGTTCGGGTCTCTGGACACAG
180
S G G G P R F L W Q P K R E C H F F N G T E R V R F L D R
40
---linker---
TACTTCTATAACCAAGGAGGAGTCCGTGGCTTCGACAGCGACGTGGGGGAGTTCGGGGCGGTACGGAGCTGGGGCGCTGACGGTGG
270
Y F Y N Q E E S V R F D S D V G E F R A V T E L G R P D A E
80
TACTGGAACAGCCAGAAGACATCCTGGAGCAGCGCGCGCGGTGGACACCTACTCTCAGACACAACACTACGGGGTGTGGAGAGCTTC
360
Y W N S Q K D I L E Q A R A A V D T Y C R H N Y G V V E S F
100
ACAGTGCACCGCGAGTCATCAAGAAGAACATGTGATCATCCAGCGCGAGTTCATCTGAATCCTGACCAATCAGCGGAGTTATGTTT
450
T V Q R R V I K E E H V I I Q A E F Y L N P D Q S G E F M F
130
GACTTTGATGTCATGAGATTTTCCATGTGGATATGGCAAGAAGAGACGGTCTGGCGGCTTGAAGAATTTGGACGATTTGCCAGCTTT
540
D F D G D E I F H V D M A K K E T V W R L E E F G R F A S F
160
GAGGCTCAAGTGCATTGCCCAACATAGCTGTGGACAAGCCAACTTGGAAATCATGACAAGCGCTCCAACATACTCCGATCACCBAAT
630
E A Q G A L A N I A V D K A N L E I M T K R S N Y T P I T N
190
XhoI
TAACTCGAG

end

FIG. 13

FIG. 14

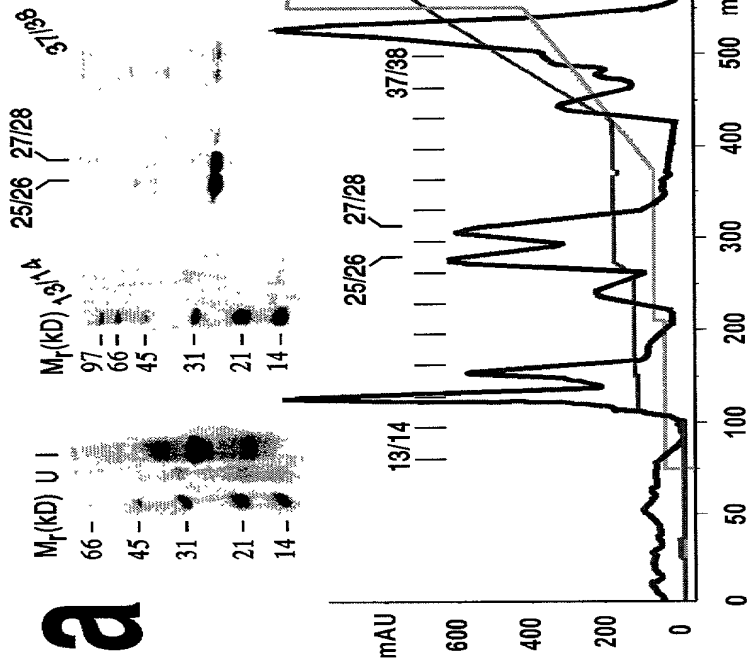
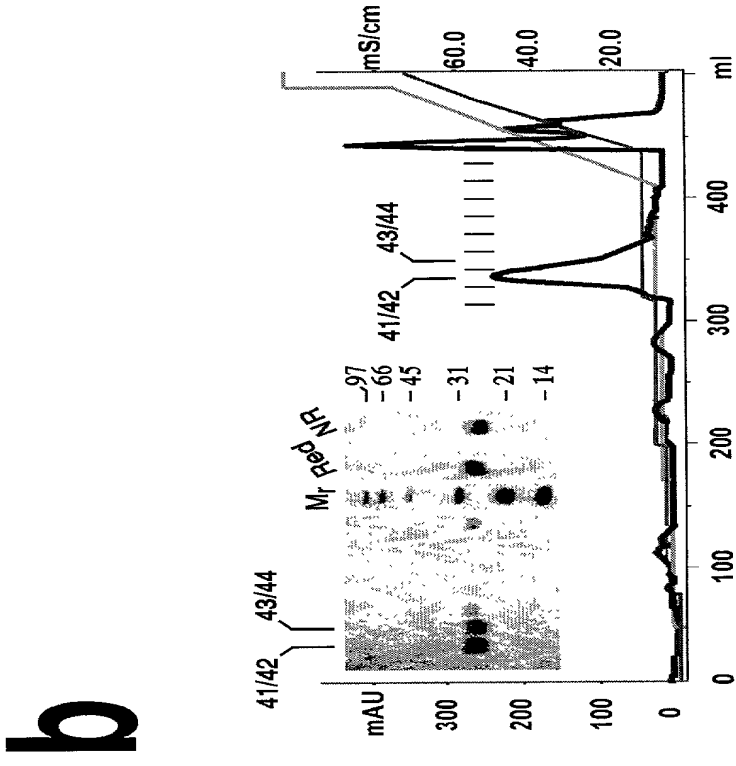


FIG. 14



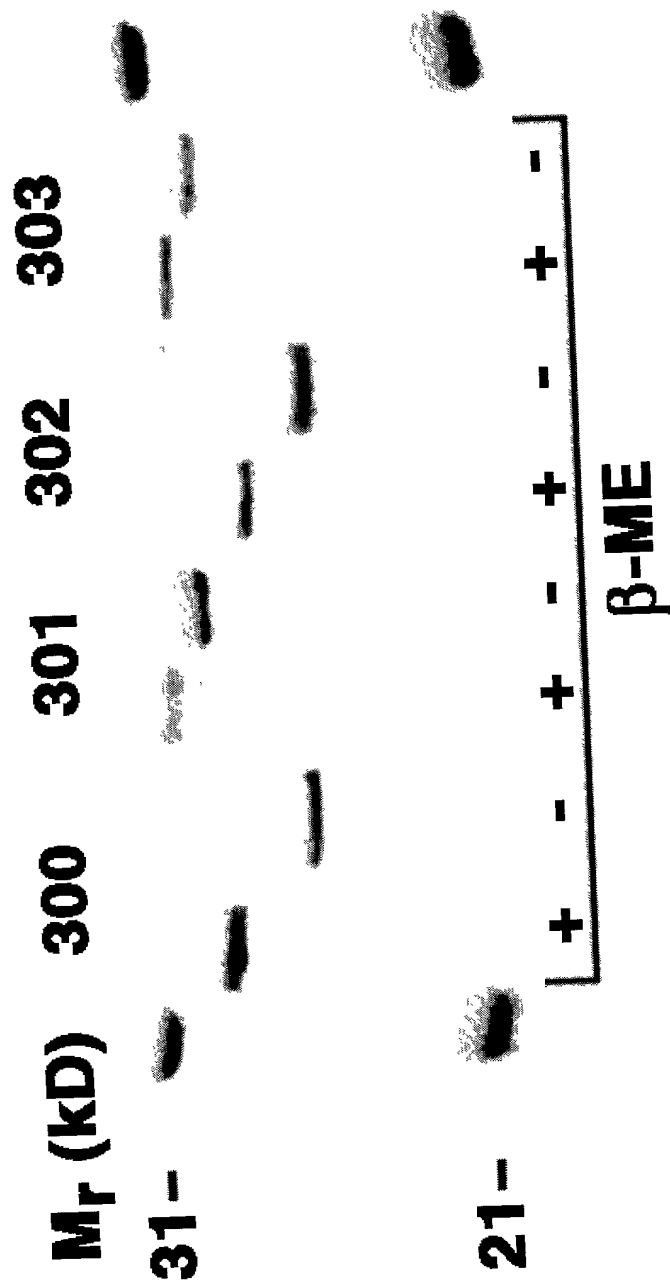


FIG. 15

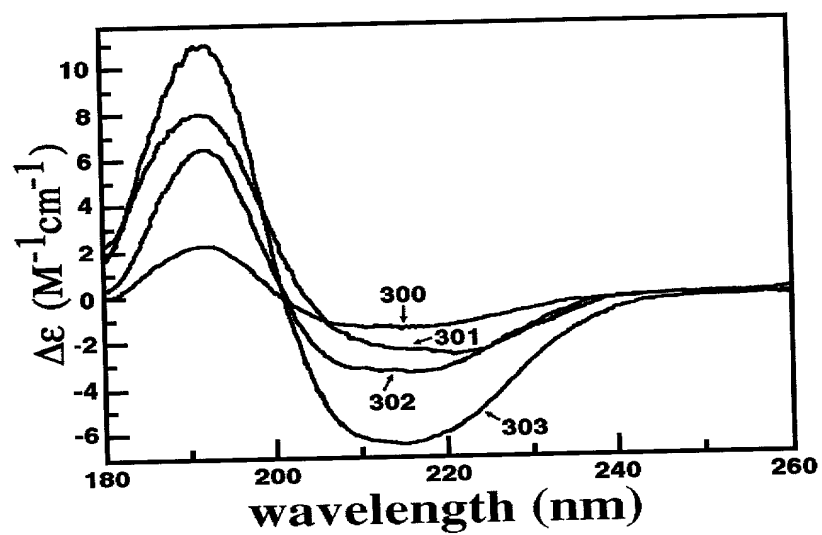


FIG. 16

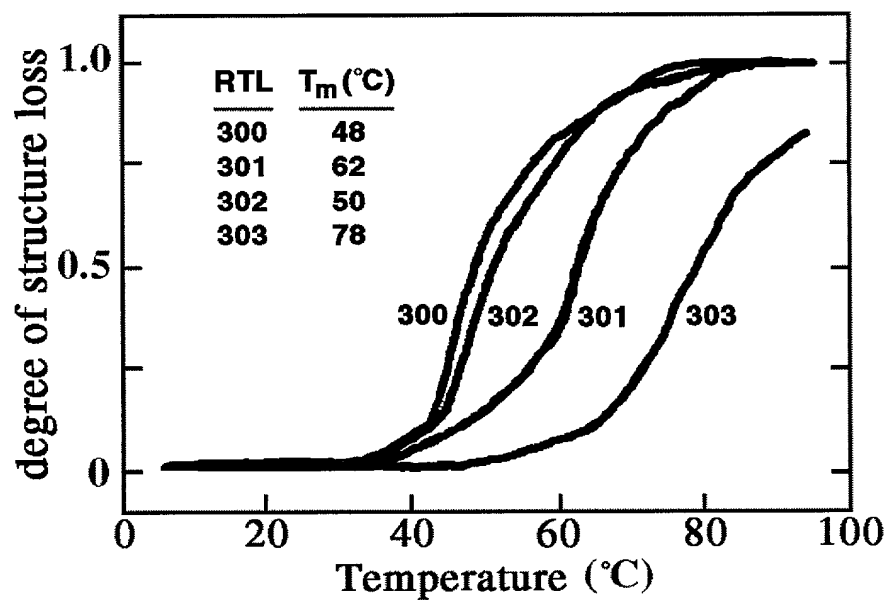


FIG. 17

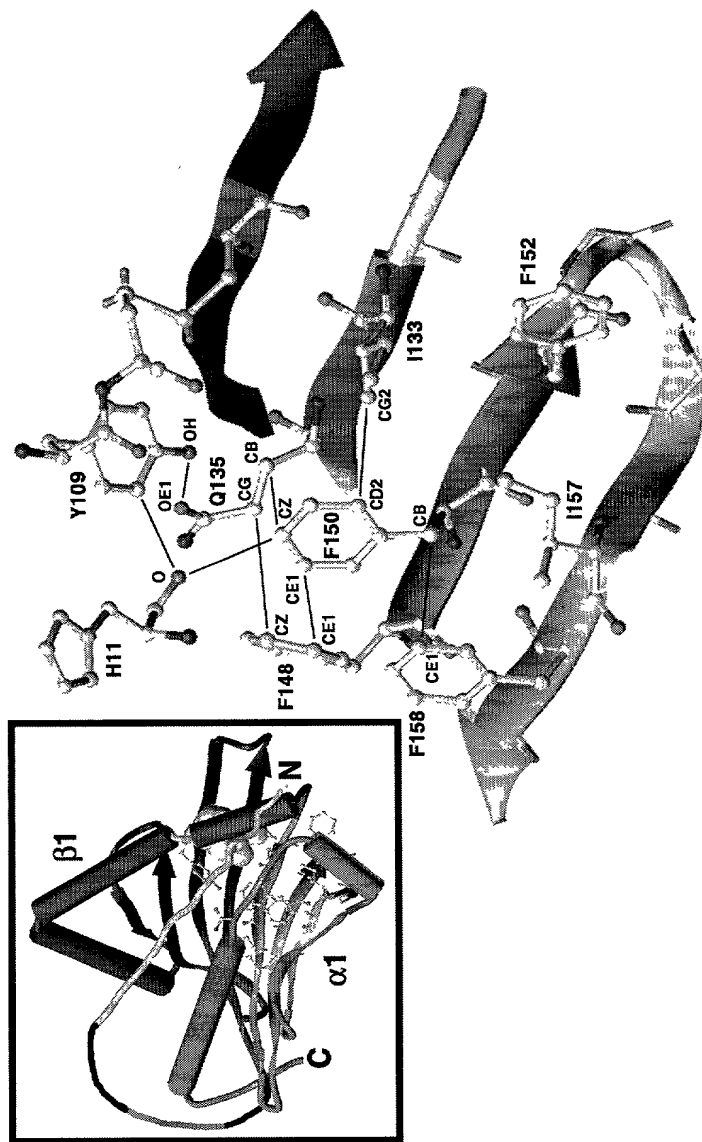


FIG. 18

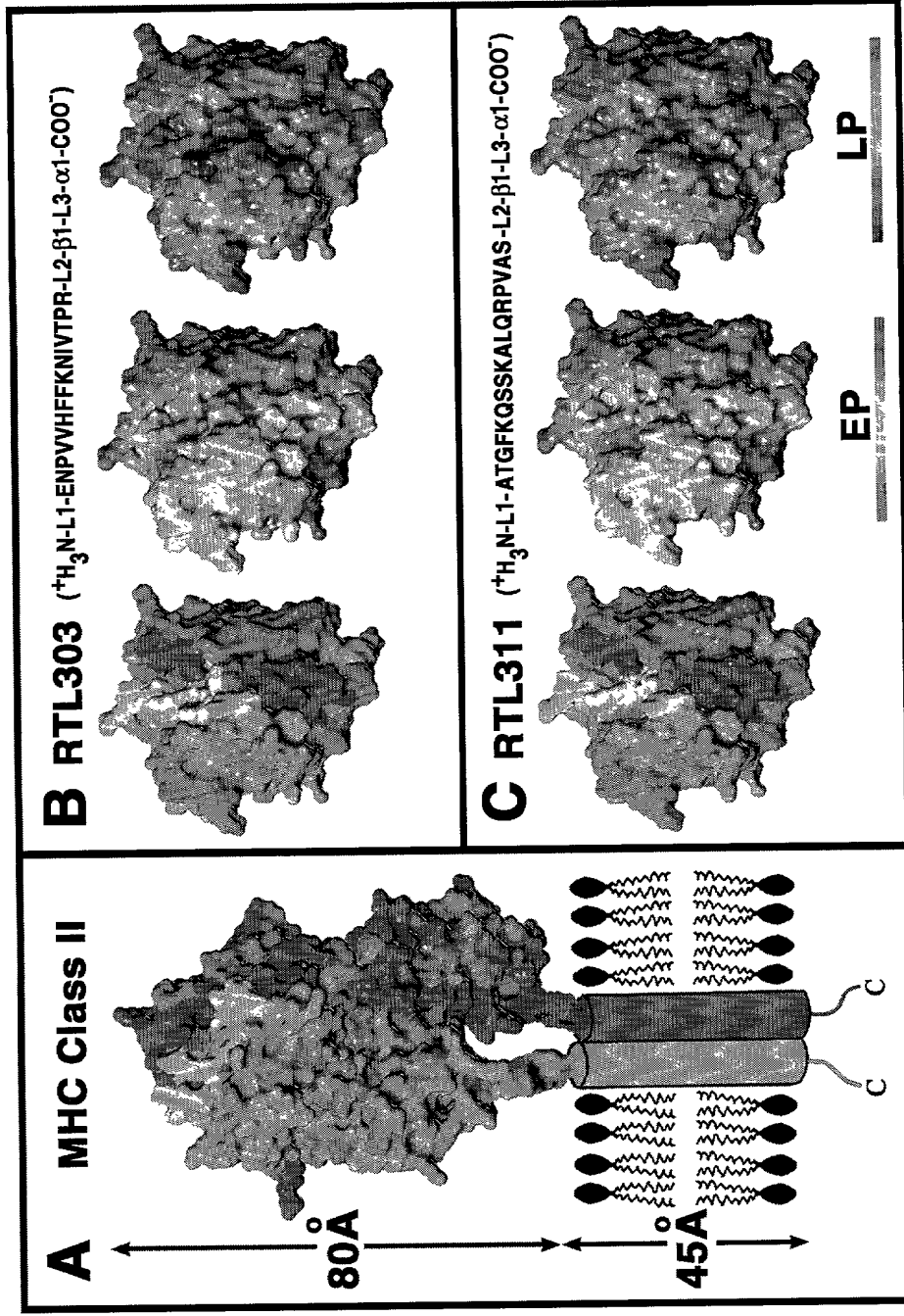


FIG. 19

MR#3-1 MR#2-87 CP#1-15

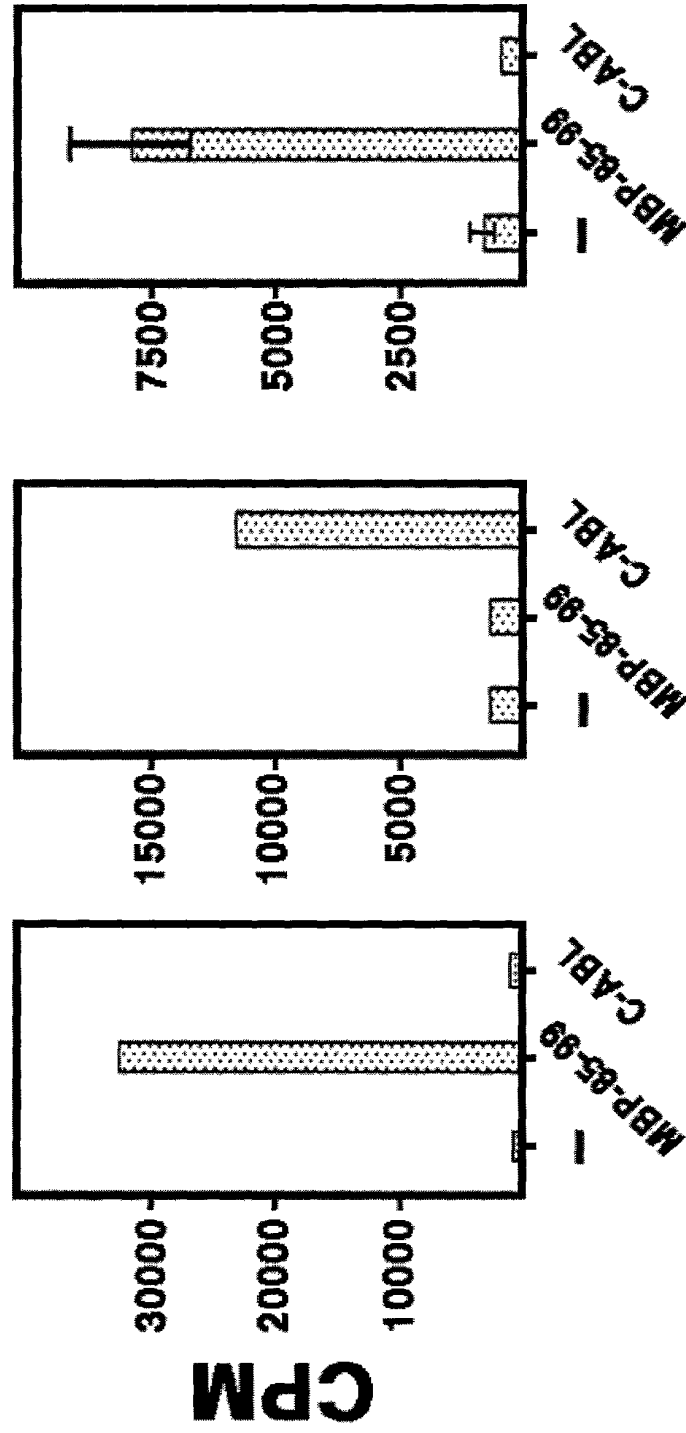
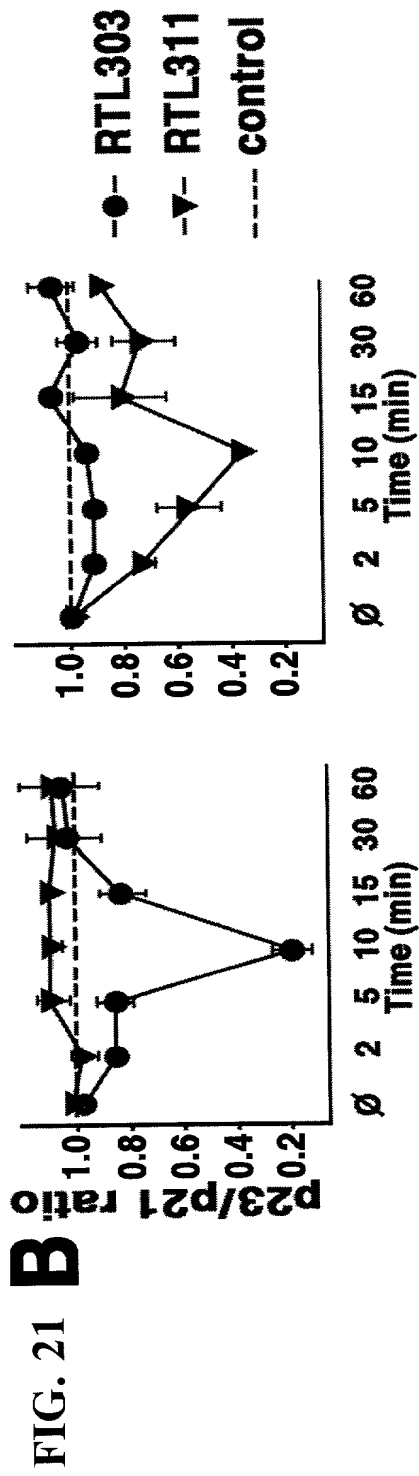
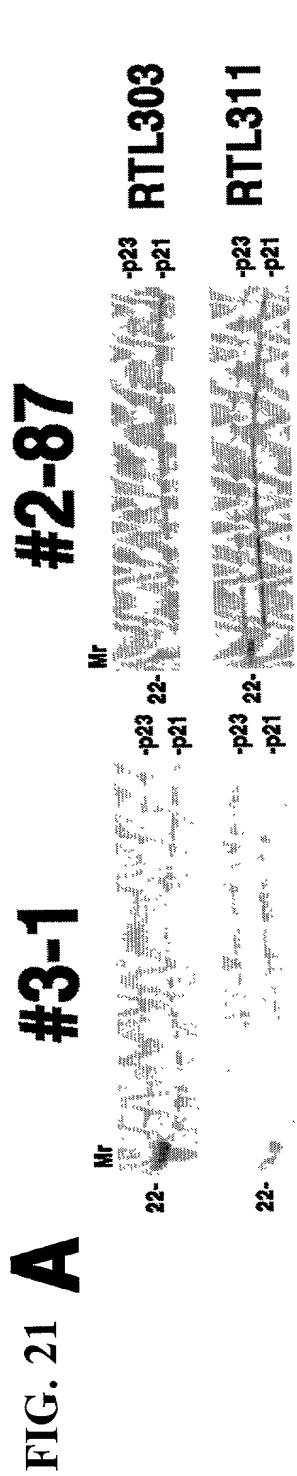


FIG. 20



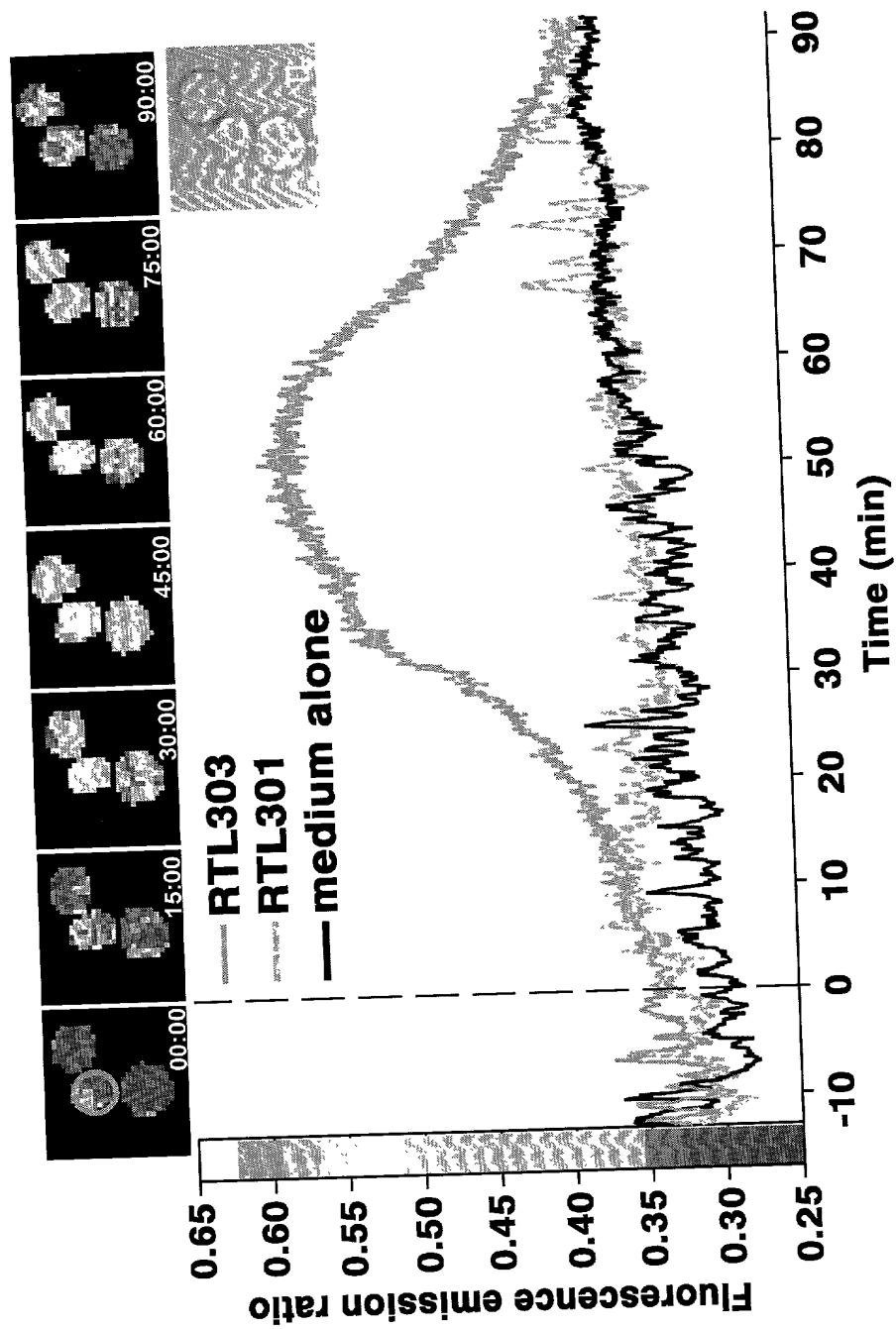


FIG. 22

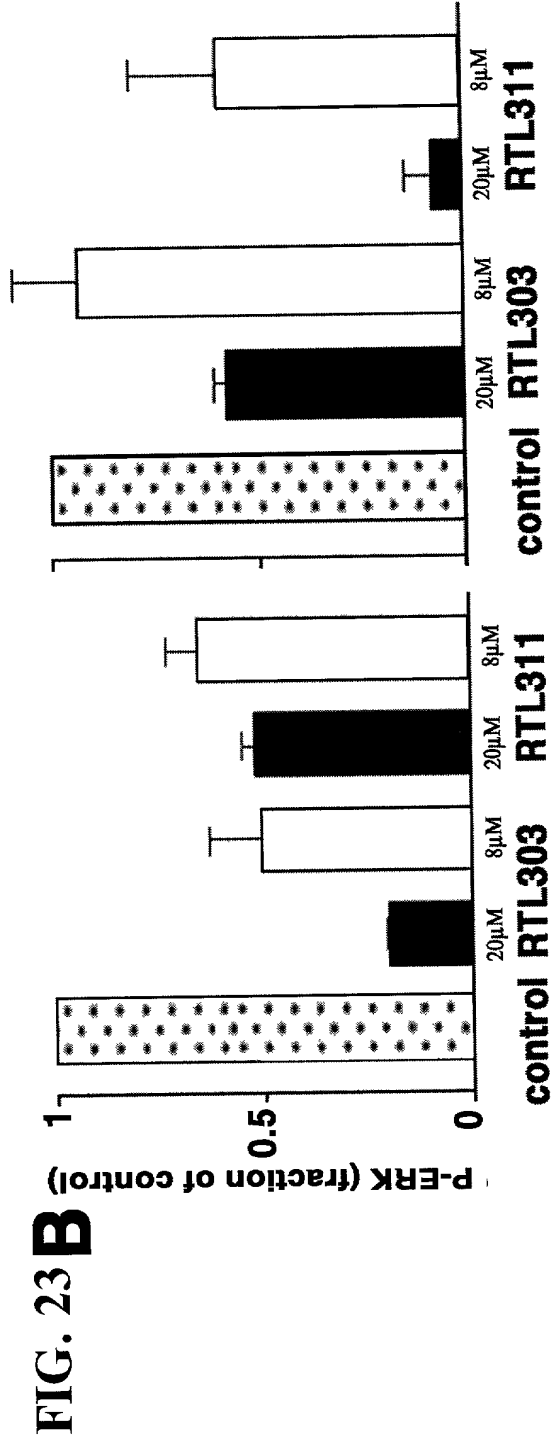


FIG. 24 A MR#3-1

FIG. 24 A MR#3-1

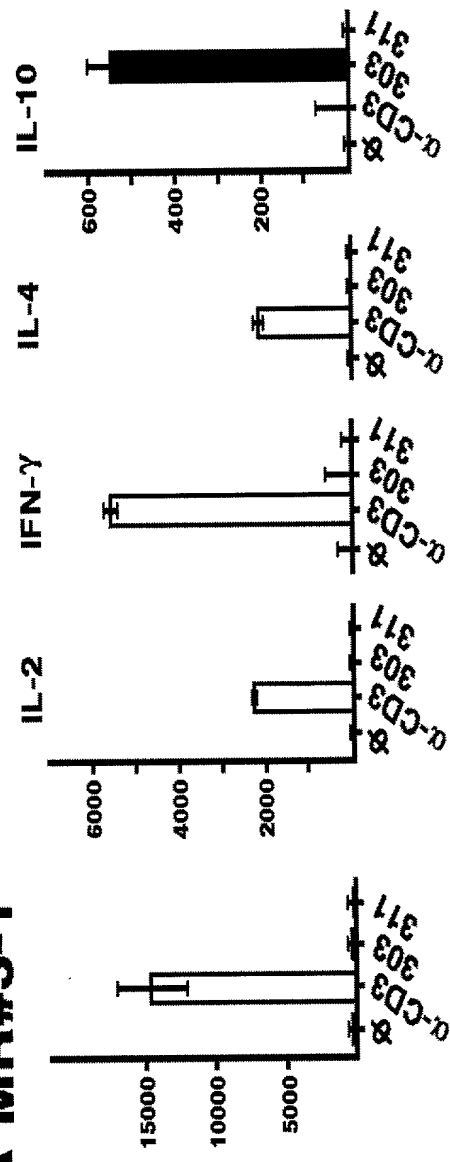


FIG. 24 B MR#2-87

